

89. The method of claim 88 wherein said agent is administered at a dose of about 100 mg/kg of body weight.

REMARKS

Claims 1-24, 28-30, 35-38, 40, 42-70 and 75 have now been cancelled without prejudice. A complete set of claims presently pending in this application, namely claims 71-74 and 76-89, are listed above. Claim 75 has been cancelled as being a substantial duplication of claim 74.

The Title of the application has now been changed in order to conform more closely to the present claims in light of the restriction requirement.

The section of the application dealing with the relationship of the present case to prior applications has also been changed to properly reflect the status of the prior applications.

The application has also been perused in order to correct obvious typographical errors and errors in trademark identifications. Applicant was unable to find any obvious trademarks which should have been previously noted. If the Examiner is aware of any such items, please advise the undersigned. The typographical errors in claims 71 and 80 have been corrected as requested.

Claims 50, 51, 60-67 and 71-85 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to contain an adequate written description of the invention as now claimed. In particular, the Examiner states that the specification does not support the claimed chimeric embodiments of the invention. The Examiner states that this is both a new matter and a written description rejection. This rejection is respectfully traversed.

In response to the Examiner's suggestion that applicant identify the portions of the specification which refer to chimeric constructs, applicant points to page 9, lines 4-5, which specifically recite such constructs with other molecules.

Notwithstanding, in the interest of advancing the prosecution of this application, this particular embodiment has now been cancelled without prejudice to presenting claims to this embodiment in related application.

Claims 13, 24, 42, 43, 45, 48-52, 60-67, 71-81 and 83-85 have been rejected under 35 U.S.C. 112, first paragraph, as lacking enablement. The Examiner states that the specification fails to provide adequate enablement for any fragment or analog of PSG1. In contrast, the

Examiner acknowledges that the specification is enabling for fragments and analogs that inhibit the interaction of P-selectin and PSGL-1. It is noted that claim 83, which is directed to PSGL-1, has not been rejected on this basis. This ground of rejection is also traversed

In response, applicant notes that the claims explicitly provide that the agents of the invention inhibit the interaction between P-selectin and a ligand of P-selectin, and E-selectin and a ligand of E-selectin. Accordingly, and contrary to the Examiner's assertion, the present claims do not cover any fragment or analog of PSGL-1, but only those fragments and analogs which inhibit P-selectin and ligand binding. See page 7, lines 30-35. The claimed fragments and analogs must be capable of inhibiting the interactions stated in the claims. Thus, the fragments and analogs of the invention are defined in terms of both structure and function, and fully comply with the enablement requirements of 35 U.S.C. 112.

Claims 1-4, 6-14, 17, 21, 22, 24, 44, 45, 48, 49, 52, 54 and 71-82 stand rejected under 35 U.S.C. § 102(e) as being anticipated by the Cummings et al. reference (U.S. Patent No. 5,464,778). Claims 1-4, 6-14, 17, 21, 22, 24, 35-37, 42, 43, 45, 48-52, 54-57, 60-67 and 71-85 also stand rejected under 35 U.S.C. 103(a) as obvious over the Cummings et al. reference (U.S. Patent No. 5,464,778) in view of the Larsen et al. reference (U.S. Patent No. 5,840,679). These grounds of rejection are traversed.

The Examiner states that Cummings et al. teaches the use of PSGL in the treatment of leukocyte adherence, inflammation and coagulation. The Examiner contends that the inhibition of P-selectin, E-selectin and ligand interaction is an inherent property of PSGL. Further, the Examiner states that Larsen et al. teaches chimeric forms of PSGL, such as antibodies, which are used to treat inflammatory and thrombolytic conditions.

Neither the Cummings et al. nor the Larsen et al. references recognize the role of P-selectin in the formation of atherosclerotic lesions, or teach or suggest the use of PSGL to prevent the formation of the lesions, i.e. to prevent atherosclerosis. Cummings et al. is directed to a novel ligand of P-selectin derived from myeloid cells. Cummings et al. teach that antibodies to the ligand can be used to block binding to the ligand on leukocytes, thus inhibiting inflammation.

In contrast, and as explained in the present specification, the formation of atherosclerotic lesions is the result of the binding of monocytes and T lymphocytes to the surfaces of endothelial cells in the lumen of the artery wall. These cells form the lesions known as fatty streaks, which in turn develop into fibrous plaques. See pages 1 and 2 of the specification. Applicants have

discovered that P-selectin is involved in the formation of atherosclerotic lesions, and that a therapeutic agent which inhibits the binding of P-selectin and P-selectin ligand can be used to treat atherosclerosis.

Although the Examiner states that the references describe the use of PSGL to treat inflammation, the prior art does not recognize any relationship between inflammation and atherosclerosis. Applicants were the first to recognize that PSGL-1 could be used to treat atherosclerosis. Consequently, one skilled in the art would not have been motivated to use PSGL-1 as a therapeutic for the treatment of atherosclerosis since (1) there is no connection between atherosclerosis and the other, unrelated disease states mentioned in the references, and (2) there would be no motivation or reasonable expectation that such a treatment would have succeeded. For these reasons, among others, applicants maintain that the references fail to teach or suggest the atherosclerosis treatment method of the present invention.

Claims 1-4, 6-14, 17, 21, 22, 24, 35-37, 42, 43, 45, 48-52, 54-57, 60-67 and 71-85 have been rejected under the doctrine of obviousness-type double patenting in view of claims 40-41, 45, 49-52, 56, 59-60, 63-74 of copending U.S. application no.09/436,076, and claims 39-88 of U.S. application no. 09/883,642.

Without conceding the propriety of this rejection, applicant notes that this is a provisional-type double patenting rejection which can be overcome by filing a terminal disclaimer. Applicant would be prepared to file a terminal disclaimer in this application to overcome this rejection provided that the application is otherwise considered to be in proper condition for allowance.

In view of the foregoing facts and reasons, the present application is now believed to overcome the remaining rejections, and to be in proper condition for allowance. Accordingly, reconsideration and withdrawal of the rejections, and favorable action on this application, is solicited. The Examiner is invited to contact the undersigned at the telephone number listed below to discuss the status of this application if necessary.

Respectfully submitted,

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MARKED-UP CLAIMS

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71. A method for treating or inhibiting atherosclerosis in a mammal comprising:
providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin; and
administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of PSGL-1, soluble forms of PSGL-1, fragments of PSGL-1, and mimetics of PSGL-1 [or a fragment thereof, and chimeric constructs of PSGL-1 or a fragment thereof].
80. The method of claim 78 wherein said [leu8kocyte] leukocyte is a monocyte.

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